Available online at www.sciencedirect.com
ScienceDirect
EJSO
the Journal of Cancer Surgery
ELSEVIER
EJSO 36 (2010) 463–469
www.ejso.com

Cost analysis of the combined procedure of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC)

D. Baratti [a], A. Scivales [b], M.R. Balestra [a], P. Ponzi [b], F. Di Stasi [b], S. Kusamura [a], B. Laterza [a], M. Deraco [a,*]

[a] *Department of Surgery, National Cancer Institute, Via Venezian, 1, 20133 Milan, Italy*
[b] *Medtronic Italia, Piazza Montanelli, 30, 20099 Sesto San Giovanni (MI), Italy*

Accepted 15 March 2010
Available online 2 April 2010

Abstract

Aim: The aim of the present study was to address the economic cost of the innovative comprehensive approach involving cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) to treat peritoneal surface malignancies, and to compare it with the financial support received by our centre.
Methods: A retrospective economic analysis was carried out on 382 consecutive procedures performed at a tertiary referral centre during the period 1995–2008. The costs of the combined therapy were estimated using the activity-based costing methodology. The financial support was assessed according to the current diagnosis-related group classification and reimbursement rates.
Results: The mean cost for one hospital stay was €36,015.89 (range 28,435.24–82,189.08); mean length of stay was 24.3 days (range 9–108). In counterpart, our hospital received a total financial support of €804,483.30, resulting in a deficit of €1861,301.99 for the two years.
Conclusion: The Italian current diagnosis-related groups classification does not include cytoreduction and HIPEC. This results in a relevant economic deficit for the hospitals offering this treatment option to their patients and a slow diffusion of the technique in our country. Two corrective measures are needed: to include this procedure in the official list of medical acts, and to determine its specific cost for reimbursing.

Keywords: Peritoneal surface malignancies; Cytoreductive surgery; Hyperthermic intraperitoneal chemotherapy; Costs; Diagnosis related group; HIPEC

Introduction

Peritoneal surface malignancy (PSM) refers to a group of conditions in which the intra-abdominal tumour spread is the dominant clinical picture. These include carcinomatosis of gastro-intestinal and gynecological origin and rare primary peritoneal tumours, such as peritoneal mesothelioma and the exceedingly uncommon primary peritoneal (extra-ovarian) carcinoma.[1] PSM were once regarded as end-stage metastatic conditions only amenable to palliative options. Over the last two decades, these disease entities have been increasingly recognized as a manifestation of local-regional disease spread and, accordingly, an aggressive local-regional treatment approach has emerged.[1] This innovative strategy involves peritonectomy procedures and multivisceral resection to remove the macroscopic tumour, in combination with perioperative intraperitoneal chemotherapy to sterilize microscopic residual disease.[2]

Several independent trials of cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC) have reported a dramatic survival improvement in selected patients with various PSM.[3–8] Although pseudomyxoma peritonei is minimally aggressive, long-term survival after conventional debulking surgery and palliative chemotherapy was only 20–30%. With the advent of the local–regional approach, it has increased to 52–96%, and median survival to 51–156 months.[3] Analogously, median survival has improved from about 12 to 34–92 months for peritoneal mesothelioma and from 6 to 12–33 months for colorectal cancer carcinomatosis.[4,5] In stage-III ovarian cancer, complete surgical cytoreduction has

* Corresponding author. Tel.: +39 02 23902362; fax: +39 02 23902404.
E-mail address: marcello.deraco@istitutotumori.mi.it (M. Deraco).

0748-7983/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejso.2010.03.005

been shown to be closely related to survival and a phase-III study has demonstrated the survival benefit of intraperitoneal versus intravenous chemotherapy, supporting the use of the combined treatment in this clinical setting.[6–8] Results of cytoreduction and HIPEC in our Institution were reported previously: median survival was 41.4 and 44 months for ovarian cancer and peritoneal mesothelioma, and 79.4% at ten years for pseudomyxoma peritonei.[9–11]

Since the comprehensive approach was developed by Sugarbaker, many peritoneal malignancy treatment centres have been established in the USA, Japan, Australia and Europe. However, this treatment option is highly resource-expensive, requiring specialized surgical teams, complex technological facilities and long operative times. Although a few economic evaluations are available in the literature, costs have never been assessed in Italy, resulting in a slow diffusion of this technique in our country. Therefore, we have investigated the economic costs of cytoreduction and HIPEC in an Italian tertiary referral centre and compared costs with the reimbursement rates for these acts, according to the current diagnosis-related grouping (DRG) classification.

Materials and methods

Study design

The economic evaluation was based on 382 procedures of cytoreduction and HIPEC performed in 376 patients by the same surgical team at the National Cancer Institute (NCI) in Milan (Italy) during the period 1995–2008. Milan NCI is a comprehensive cancer centre and the Italian reference institution for PSM management. The total cost of each hospital admission was assessed according to present day (2007) unit costs (e.g. cost of 1 mg of chemotherapy agents, cost of 1 min of operating room occupation). This methodology was applied to ensure both an updated economic evaluation and a larger database covering a wide spectrum of clinical settings. A comparison between the costs sustained and the financial support received in counterpart by our hospital was made for the last two years of the study period, when the number of procedures performed stabilized steadily at 35–40/year. Patient characteristics are shown in Table 1.

Operative treatment

All patients included in this study were treated according to institutionally approved protocols with written informed consent. Eligibility requirements included: histological diagnosis of PSM; age $\leq$75; no relevant co-morbidities; Eastern Cooperative Oncology Group performance status $\leq$2[12]; no hepatic or distant metastasis; peritoneal disease amenable to complete/near-complete cytoreduction at preoperative computed tomography scan.

Cytoreductive surgery was based on the technique originally described by Sugarbaker,[2] with some modifications.[13] Briefly, the aim of the surgical cytoreduction was to remove all the visible peritoneal tumour by one to six of the following steps: right parietal peritonectomy ± right colectomy; pelvic and left parietal peritonectomy ± sigmoidectomy ± hysteroadnexectomy; lesser omentectomy and duodenal–hepatic ligament dissection ± cholecystectomy; right diaphragmatic

Table 1
Clinical characteristics of 376 patients with peritoneal surface malignancies.

		Overall series (n = 376)	Years 2007–2008 (n = 73)
Sex	Male	133	27
	Female	243	46
Median age, years (range)		55 (22–81)	54 (28–76)
PSM	Pseudomyxoma peritonei	138	35
	Peritoneal mesothelioma	110	28
	Ovarian cancer carcinomatosis	51	5
	Colorectal cancer carcinomatosis	18	2
	Gastric cancer carcinomatosis	12	–
	Papillary serous carcinoma	4	2
	Abdominal sarcomatosis	37	–
	Other	6	1
ECOG score	0	309	54
	1	57	15
	2	10	–
Previous surgery	Only biopsy	138	26
	1 Abdominal region dissected	136	17
	2–5 Abdominal regions dissected	98	28
	>5 Abdominal regions dissected	4	2
Previous syst. chemotherapy	Done	171	27
	Not done	275	46
Mean PCI (range)		19.2 (3–39)	21.9 (3–39)

PSM: peritoneal surface malignancy; ECOG: Eastern Cooperative Oncology Eastern Group; PCI: peritoneal cancer index.

peritonectomy ± Glisson's capsulectomy; greater omentectomy, left diaphragmatic peritonectomy ± splenectomy; gastric antrectomy/total gastrectomy ± other intestinal or abdominal mass resections. The extent of peritoneal involvement was rated at surgical exploration using the peritoneal cancer index (PCI).[14]

The HIPEC was performed according to the closed-abdomen technique using two in-flow and two out-flow catheters. The extracorporeal circulation device Performer LRT® (RAND, Medolla [MO], Italy) was used. The HIPEC drug schedules were: cisplatin (25 mg/m^2/L) with mitomycin-C (3.3 mg/m^2/L) for 60 min to treat pseudomyxoma peritonei, gastric and colorectal carcinomatosis[15]; cisplatin (43 mg/L) with doxorubicin (15.25 mg/L) for 90 min to treat peritoneal mesothelioma, abdominal sarcomatosis and ovarian carcinomatosis.[16] A 30% dose reduction was applied to patients older than 70 years or with previous chemotherapy and/or extensive surgical cytoreduction. In-flow temperature was 44 °C to maintain an intra-abdominal temperature of 42.5 °C

Following surgery, patients were admitted to the intensive care unit (ICU) to be continuously monitored. Laboratory and instrumental exams were performed daily. They were then discharged to the surgical ward for recovery. Laboratory exams were performed every three days until discharge. Postoperative complications occurring during the hospital stay were rated according to the National Cancer Institute Common Terminology Criteria (http://ctep.cancer.gov/forms/CTCAEv3.pdf).

Cost assessment

Cost assessment focused on inpatient care. The activity based costing (ABC) methodology was applied to estimate hospital costs.[17] A detailed assessment of all expenditures in terms of materials used, drugs administered, pre- and postoperative examinations, professionals involved, equipment amortization, time spent in the operating theater, days spent in ICU and surgical ward was carried out.

Information on patient and treatment characteristics, length of hospital and ICU stay, type and dosage of drugs administered during the HIPEC, blood product consumption were collected from a prospective clinical database specifically designed for patients with PSM. According to ABC principles, data on resource consumption were retrieved by detailed interviewees with medical and nurse staff. Costs of ancillaries and disposal materials were derived from tender adjudication prices. The remaining daily costs of hospitalization (i.e. daily costs of hospital bed occupancy), were provided by the Accounting Department as €200.00 for the surgical ward and €2,500.00 for the ICU. The operating room register provided information on the number of professionals involved in the combined procedure and the time spent in the theater by each of them. Human staff-related cost of the surgical intervention was then obtained by multiplying the unit cost per minute by the operative time. Non-staff cost per minute was added to cover running costs of the operating theater. The costs of reoperations for postoperative complications during the same stay were added to the first operation. Equipment amortization was calculated by dividing the acquisition cost by the number of procedures carried out in four years (40 per year). Investigations performed before and after intervention were valued by tariff set for inpatient services in Lombardia Region. Type and dosage of medications administered during the hospital stay were assessed considering the ward clinical practice; their costs were estimated by acquisition cost, according to the Drug Formulary (2007–2008). Finally, overhead costs were added as a 13% percentage of the measured costs, according to the indications of the Accounting Department.

Once the mean cost of one hospital stay for cytoreduction and HIPEC was estimated, we conducted a subanalysis according to a three-tiered classification of the complexity of the cytoreduction: level 1 (1–2 cytoreductive surgical procedures), level 2 (3–4 procedures) and level 3 (5–6 procedures).

Reimbursement rates

According to the official classification at the time of the study in Lombardia region, the stays for cytoreduction and HIPEC were categorized in two DRGs:

- DRG 148: major small and large bowel surgical procedures, with complications (for whom our hospital received €9,632.70).
- DRG 408: poorly differentiated tumour undergoing major surgical procedures, with complications (for whom our hospital received €13,557.60).

Results

Clinical data

The details of the combined procedures are displayed in Table 2. Operative mortality occurred in 8 patient (2.1%), and grade 3/5 surgical complications in 70 (18.3%); reoperation rate was 50/382 (13.1%). Bone-marrow toxicity occurred in 23 patients and renal toxicity in 22. Overall, 95 patients (24.8%) suffered of grade 3/5 adverse events.

The mean hospital stay was 24.3 days (range 9–108); in detail, median preoperative stay was one day (range 1–3), postoperative ICU stay 3 days (range 2–15) and surgical ward stay 18 days (range 7–91). Average operative time was 550 min (range 240–1240). Further analyses were performed according to the complexity of the procedure. Mean hospital stay was 19.7 days (range 15–24) and mean operative time was 388 min (range 240–660) in 57

Table 2
Cytoreductive surgical procedure and HIPEC data.

	Overall series ($n = 382$)	Years 2007–2008 ($n = 73$)
Peritonectomy procedures		
Right upper quadrant	254	72
Left upper quadrant	257	69
Pelvic	287	67
Greater omentectomy	310	68
Lesser omentectomy	246	63
Mean	3.54	4.64
Median (range)	5 (1–5)	5 (1–5)
Visceral resection		
Glisson's capsule resection	118	14
Cholecistectomy	123	35
Partial/total gastrectomy	17/32	7/4
Splenectomy	203	58
Right colectomy	147	27
Appendectomy	57	16
Sigmoidectomy	156	41
Subtotal/total colectomy	11	5
Small bowel resection	75	20
TAH-BSO	68	20
Other	86	18
Protective ostomy	23	10
Mean	2.92	3.61
Median (range)	3 (0–9)	4 (0–8)
Completeness of cytoreduction		
No visible residual tumour	227	22
Residual tumour ≤2.5 mm	117	38
Residual tumour >2.5 mm and ≤25 mm	23	7
Residual tumour >2.5 mm	15	5
HIPEC drug schedule		
Cisplatin + mitomycin-C	223	38
Cisplatin + doxorubicin	159	35
Mean cisplatin dose, mg (SD)	193.8 (46.5)	179.8 (38.3)
Median (range)	200 (100–300)	180 (90–280)
Mean mitomycin-C dose, mg (SD)	28.8 (7.5)	27.1 (5.6)
Median (range)	30 (15–90)	25 (15–40)
Mean doxorubicin dose, mg (SD)	64.8 (14.1)	68.6 (14.29)
Median (range)	60 (25–90)	63.5 (40–90)

HIPEC: hyperthermic intraperitoneal chemotherapy; TAH: total abdominal hysterectomy; BSO bilateral salpingo-oophorectomy; SD: standard deviation.

level 1 procedures. For 152 level 2 and 173 level 3 procedures, mean hospital stay was 20.4 (range 10–50) and 25.1 (9–108) days; mean operative time was 502 (range 240–930) and 601 min (330–1260) minutes, respectively.

Economic costs

The mean total cost of one hospital stay for cytoreduction and HIPEC was €36,015.89 (range 28,435.24–82,189.08) In Table 3, the main cost items are detailed. The costs of the procedure was analyzed by dividing the hospital stay into three phases (the procedure itself, preoperative and postoperative stay) and by resource: €2211.15 (6%) were related to the preoperative phase, €19,927,25 (55%) to the operative procedure and €13,877.49 (39%) to the postoperative phase.

Table 3
Mean costs of the combined procedure of cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC).

Item	Cost
Preoperative stay	€ 200.00
ICU stay	€ 7,500.00
Postoperative stay	€ 3,600.00
Total hospital stay	€ 11,300.00
Preoperative investigations	€ 138.85
Medications	€ 1,622.92
Operating room occupation	€ 7,273.55
Personnel	€ 2,360.06
Disposal materials	€ 1,980.56
Equipment amortization	€ 450.00
HIPEC disposal devices	€ 2,909.49
HIPEC drugs	€ 649.73
Blood products	€ 2,006.34
Total surgical combined intervention	€ 17,629.73
Postoperative care	€ 1,180.96
Overhead costs (13%)	€ 4,143.42
Total	€ 36,015.89

ICU: intensive care unit; HIPEC: hyperthermic intraperitoneal chemotherapy.

The only hospital stay (both pre- and postoperative) accounted for €12,769.00 (35%) and the staff for €9082.19 (25%). The third most relevant cost item was pharmacological therapy (including drugs administered during the HIPEC), accounting for €7293.84 (20%). The additional cost due to disposable materials for the HIPEC was €2101.80 (6%).

Procedure costs were evaluated according to the complexity of the surgical cytoreduction. The mean costs of level 1, 2 and 3 procedures and their breakdown into cost components are shown in Table 4. The total cost of the hospital stay seems to be most closely related to the costs of the operative procedure and, to a lesser extent, to hospitalization costs. This may be explained by the fact that operative time increased with the complexity of the surgical

Table 4
Mean cost of the combined procedure of cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC), according to the extent of the cytoreductive surgery.

	Level 1	Level 2	Level 3
Hospital stay	€ 12,317.00	€ 12,317.00	€ 13,321.00
Preoperative investigations	€ 156.90	€ 156.90	€ 156.90
Medications	€ 1,833.89	€ 1,833.89	€ 1,833.89
Surgery	€ 17,112.95	€ 18,948.63	€ 20,542.78
Postoperative care (excluding hosp. stay)	€ 1,334.48	€ 1,334.48	€ 1,334.48
Estimated hospital stay cost	€ 32,755.24	€ 34,590.92	€ 37,089.07

Level 1: 1–2 cytoreductive surgical procedures; level 2: 3–4 procedures; level 3: 5–6 procedures.

cytoreduction and, consequently, costs of staff involvement and operating theater occupancy proportionally increase. All other costs seem to hold steady. In a further analysis, staff-related costs were the only resource proportionally increasing with complexity level. For level 1, 2 and 3 procedures, staff accounted for 19.1%, 23.4% and 25.9%, respectively, of the total costs of stay (data not shown).

Reimbursement analysis

During the period 2007–2008, four level 1 combined procedures accounted for a total cost of €131,020.96 (€32,755.24 × 3). Ten level 2 procedures accounted for of €345,909.20 and 59 level 3 procedures for €2,188,255.13. Therefore, the total cost for the two years was €2,665,185.29. Thirty-five combined procedures for pseudomyxoma peritonei and 2 for colorectal carcinomatosis were classified in the DRG 148, resulting in a total financial support of €356,409.70. Thirty-eight procedures for peritoneal mesothelioma, ovarian carcinomatosis, primary peritoneal carcinoma and cervical cancer carcinomatosis were classified in the DRG 406, resulting in a total financial support of €448,073.60. The total reimbursement for the two years was €804,483.30, resulting in a deficit of €1,861,301.99.

Discussion

In the present analysis, the costs of the combined treatment of surgical cytoreduction and HIPEC were assessed in an Italian tertiary referral centre. Based on 382 consecutive procedures carried out in the period 1995–2008, the estimated mean cost for one procedure was €36,015.89. As compared with the financial support received by our hospital, this resulted in an economic deficit of approximately €1,850,000 for the last two years.

The main criticism against cytoreduction and HIPEC is that long-term survival has been achieved in selected case-series and modern chemotherapeutic and biologic agents for metastatic colorectal cancer might obtain comparable results in the same patients.[18] However, these drugs have never been thoroughly assessed by medical oncologists in the setting of peritoneal carcinomatosis. Furthermore, two comparative surgical studies have demonstrated the superiority of cytoreduction and HIPEC over conventional treatment: in a randomized trial, median survival was 23 months with the combined approach and 12.6 months with fluorouracil/leucovorin-based systemic chemotherapy ($P = 0.0032$).[19] In a recent retrospective controlled study, median survival was 23.9 months with modern systemic agents and an unprecedented 62.7 months with optimal cytoreduction and HIPEC ($P < 0.05$).[20] Additionally, the combined treatment has been questioned for its high complications rates, but a recent comprehensive literature review demonstrated that morbidity and mortality are comparable with major abdominal surgery.[21]

Criticisms have also involved the high economic cost of combined treatment. However, the Institut Gustave-Roussy (Villejuif, France) estimated in a retrospective controlled study the cost-effectiveness of HIPEC versus systemic chemotherapy for colorectal cancer carcinomatosis as €58,086 per life-year saved (95% confidence interval 35,893–112,839).[22] In comparison, the cost of one life-year saved is €75,000–146,000 for imatinib in unresectable gastrointestinal stromal tumour (versus supportive care) and €103,000–120,000 for trastuzumab in metastatic breast cancer (versus standard chemotherapy).[23,24]

Despite these important advancements, a peritoneal malignancy project in Italy does not receive an adequate financial support. Our current DRG classification does not include this procedure, resulting in a heavy economic deficit for the hospitals accepting the responsibility of treating these patients. Although our analysis is related to the Italian setting, information were provided which may improve the diffusion of the combined treatment in other tax-founded health systems, like in most European countries. As DRGs are updated periodically, a thorough cost assessment is the first step to obtain reimbursement rates adequate to the real cost of the procedure. An alternative solution, adopted by centres in the Netherlands and England, may be to negotiate a contract with the health authorities to finance specific cares not covered by the DRG system.[25,26] Any method of reimbursement, however, should take into the consideration that the procedure consists in a combination of surgical acts with the HIPEC. Our economic analysis demonstrated that final costs are closely related to the extent of the surgical efforts. Therefore, it seems rational to establish a total act with three different definitions: peritoneal and visceral cytoreductive surgery associated with HIPEC for peritoneal malignancy, of low, intermediate or high complexity.

Cytoreduction and HIPEC is an innovative therapy and economic evaluation are lacking. In 1996, Sugarbaker reported a total cost of the procedure of USD166,922 (range 72,795–185,464) (€116,950; range 50,760–129,324), based on 25 cases of pseudomyxoma peritonei.[27] However, this study was specific to the insurance-based USA health system and charge data were used to simulate costs, being of limited value for most European countries. The American study, together with UK price data and expert advices, was used to set a Monte-Carlo simulation model to estimate the marginal cost of the combined procedure for pseudomyxoma peritonei in the UK. The estimated cost for one patient over 5 years was 9717 pounds (€10,907), with a standard deviation (SD) of 1284 pounds (€1441).[28] These results contrast with those of the US study, since the total amount was about one-tenth of the American costs, although the studies are scarcely comparable, due to differences in the provision of the specific service. As a matter of fact, it has been recently reported that the Basingstoke Centre receive from the National Health Service 75,000 pounds per case, covering outpatient assessment, surgical treatment, follow-up and research.[19]

In France, the cost of cytoreductive surgery with HIPEC was evaluated in 73 patients treated for various PSM during 2002 and 2003.[25] Based on the hospital standard analytic accountancy, the mean cost of one hospital stay was €39,358 (SD 31,853), excluding the drugs administered during the HIPEC (€3135), which were covered by the manufacturer in the context of clinical trials. The authors analyzed the financial support given by the Health Ministry by classifying all hospital stays in twelve DRGs and according to the current rates of compensation. On average, €20,485 (range 4115–117,180) were paid, resulting in a mean deficit of €18,873 per patient and about €1,400,000 for the two years. Due to the similarity of French and Italian health services, comparable costs for both settings were estimated. Nevertheless, compensation rates in Italy were lower, accounting for a deeper economic deficit.

More recently, the costs of cytoreduction and HIPEC were assessed in Australia. In 159 procedures performed from 2002 to 2008, the average cost per procedure was 66,646 Australian Dollars (AUD) (€42,946), ranging from AUD44,668 for small bowel/ovarian cancer carcinomatosis (€28,783) to AUD92,308 for pseudomyxoma peritonei (€59,482). Based on available data on lifetime cost for colorectal cancer carcinomatosis managed with palliative therapies, the cost per life-year saved with cytoreduction and HIPEC ranged from AUD20,521 (€13,223) for peritoneal mesothelioma to AUD29,599 (€19,073) for pseudomyxoma peritonei.[29]

In the present study, economic costs were assessed according to the methodology of activity-based costing.[16] Unlike conventional costing accountancy in hospitals, which mainly focuses on services, the ABC approach focuses on activities, assuming that activities consume resources and services consume the activities. The ABC allows costs to be assessed thoroughly and correctly, since the resources used and activities performed are described precisely. Furthermore, it assigns more indirect costs into direct costs. Despite these advantages, ABC is still used in few hospitals because such a methodology is more expensive and time-consuming and requires more data than traditional costing approaches.[30] These potential drawbacks, however, were overcome by taking advantage of our prospective and exhaustive clinical database.

Some limitations of the present study must be mentioned. First, our analysis focused on inpatient care and omitted ambulatory and indirect costs, because these information were difficult to collect retrospectively.[28] The severity of PSM implies that most outpatient and inpatient care was given by highly specialized institutions and ambulatory costs can be assumed to be marginal. Second, the study did not included the costs of establishing a peritoneal malignancy management centre, such as training teams, although specialist equipment amortization was taken into account.[26] Third, additional costs for subsequent hospital stays related to HIPEC procedure, such as interventions for stoma closure, rehabilitation, disease recurrence or delayed treatment consequences, were not considered.

In conclusion, although clinical results from our and other centres demonstrate safety and efficacy of cytoreduction and HIPEC in the management of selected cases of PSM, the Italian current DRG classification does not include this therapy. Consequently, the hospitals offering this treatment option to their patients receive in counterpart an inadequate financial support. Necessary corrective measures are to include this procedure in the official list of medical acts, and to determine its specific cost for reimbursing.

Conflict of interest statement

Alessandro Scivales, Patrizia Ponzi, and Francesca Di Stasi are employee of the Medtronic Italia, Piazza Montanelli, 30, 20099 Sesto San Giovanni (MI), Italy.

Acknowledgments

This study was supported in part by grants from the Italian Association for Cancer Research (AIRC) and the Italian Health Ministry. The study sponsors had no involvement in the study design, in the collection, analysis and interpretation of data, in the writing of the manuscript, and in the decision to submit the manuscript for publication.

References

1. Sugarbaker PH. Progress in the management of carcinomatosis. *Cancer J* 2009;**15**:182–3.
2. Sugarbaker PH. Peritonectomy procedures. *Ann Surg* 1995;**221**:29–42.
3. Sugarbaker PH. New standard of care for appendiceal epithelial neoplasm with pseudomyxoma peritonei syndrome. *Lancet Oncol* 2006;**1**: 69–76.
4. Yan TD, Deraco M, Baratti D, et al. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for malignant peritoneal mesothelioma: multi-institutional experience. *J Clin Oncol* 2009;**27**: 6237–42.
5. Elias D, Gilly F, Boutitie F, et al. Peritoneal colorectal carcinomatosis treated with surgery and perioperative intraperitoneal chemotherapy: retrospective analysis of 523 patients from a Multicentric French study. *J Clin Oncol* 2010;**28**:63–8.
6. Bijelic L, Jonson A, Sugarbaker PH. Systematic review of cytoreductive surgery and heated intraoperative intraperitoneal chemotherapy for treatment of peritoneal carcinomatosis in primary and recurrent ovarian cancer. *Ann Oncol* 2007;**18**:1943–50.
7. Hennessy BT, Coleman RL, Markman M. Ovarian cancer. *The Lancet* 2009;**374**:1371–82.
8. Armstrong DK, Bundy B, Wenzel L, et al. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med* 2006;**354**:77–9.
9. Baratti D, Kusamura S, Cabras AD, Laterza B, Balestra MR, Deraco M. Lymph node metastases in diffuse malignant peritoneal mesothelioma. *Ann Surg Oncol* 2010;**17**:45–53.
10. Raspagliesi F, Kusamura S, Campos Torres JC, et al. Cytoreduction combined with intraperitoneal hyperthermic perfusion chemotherapy in advanced/recurrent ovarian cancer patients: the experience of National Cancer Institute of Milan. *Eur J Surg Oncol* 2006;**32**:671–5.
11. Baratti D, Kusamura S, Nonaka D, Cabras AD, Laterza B, Deraco M. Pseudomyxoma peritonei: biological features are the dominant prognostic determinants after complete cytoreduction and hyperthermic intraperitoneal chemotherapy. *Ann Surg* 2009;**249**:243–9.

12. Oken MM, Creech RH, Tormey, et al. Toxicity and response criteria of the Eastern Cooperative Oncology group. *Am J Clin Oncol* 1982;**5**: 649–55.
13. Deraco M, Baratti D, Kusamura S, Laterza B, Balestra MR. Surgical technique of parietal and visceral peritonectomy for peritoneal surface malignancies. *J Surg Oncol* 2009;**100**:321–8.
14. Jaquet P, Sugarbaker PH. Current methodologies for clinical assessment of patients with peritoneal carcinomatosis. *J Exp Clin Cancer Res* 1996;**15**:49–58.
15. Fujimoto S, Takahashi M, Kobayashi K, et al. Combined treatment of pelvic exenterative surgery and intraoperative pelvic hyperthermochemotherapy for locally advanced rectosigmoid cancer: report of a case. *Surg Today* 1993;**23**:1094–8.
16. Rossi CR, Foletto M, Mocellin S, et al. Hyperthermic intraoperative intraperitoneal chemotherapy with cisplatin and doxorubicin in patients who undergo cytoreductive surgery for peritoneal carcinomatosis and sarcomatosis: phase I study. *Cancer* 2002;**94**:492–9.
17. Ramsey RH. Activity-based costing for hospitals. *Hosp Health Serv Adm* 1994;**39**:385–96.
18. Khatri VP. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for colorectal cancer: a panacea or just an obstacle course for the patient? *J Clin Oncol* 2010;**28**:5–7.
19. Verwaal VJ, van Ruth S, de Bree E, et al. Randomized trial of cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy and palliative surgery in patients with peritoneal carcinomatosis of colorectal origin. *J Clin Oncol* 2003;**21**: 37–43.
20. Elias D, Lefevre JH, Chevalier J, et al. Complete cytoreductive surgery plus intraperitoneal chemohyperthermia with oxaliplatin for peritoneal carcinomatosis of colorectal origin. *J Clin Oncol* 2009; **27**:681–5.
21. Chua TC, Yan TD, Saxena A, Morris DL. Should the treatment of peritoneal carcinomatosis by cytoreductive surgery and hyperthermic intraperitoneal chemotherapy still be regarded as a highly morbid procedure?: a systematic review of morbidity and mortality. *Ann Surg* 2009;**249**:900–7.
22. Bonastre J, Chevalier J, Elias D, et al. Cost-effectiveness of intraperitoneal chemohyperthermia in the treatment of peritoneal carcinomatosis from colorectal cancer. *Value Health* 2008;**11**:347–53.
23. Wilson J, Connock M, Song F, et al. Imatinib for the treatment of patients with unresectable and/or metastatic gastrointestinal stromal tumours: systematic review and economic evaluation. *Health Technol Assess* 2005;**9**:1–142.
24. Elkin EB, Weinstein MC, Winer EP, et al. HER-2 testing and trastuzumab therapy for metastatic breast cancer: a cost-effectiveness analysis. *J Clin Oncol* 2004;**22**:854–63.
25. Bonastre J, Jan P, de Pouvourville G, Pocard M, Estphan G, Elias D. [Cost of an intraperitoneal chemohyperthermia (IPCH) related to cytoreductive surgery]. *Ann Chir* 2005;**130**:553–61.
26. Moran BJ. Establishment of a peritoneal malignancy treatment centre in the United Kingdom. *Eur J Surg Oncol* 2006;**32**:614–8.
27. Sugarbaker PH, Ronnett BM, Archer A, et al. Pseudomyxoma peritonei syndrome. *Adv Surg* 1996;**30**:233–80.
28. Bryant J, Clegg AJ, Sidhu MK, Brodin H, Royle P, Davidson P. Systematic review of the Sugarbaker procedure for pseudomyxoma peritonei. *Br J Surg* 2005;**92**:153–8.
29. Chua TC, Martin S, Saxena A, et al. Evaluation of the cost-effectiveness of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (peritonectomy) at the St George Hospital peritoneal surface malignancy program. *Ann Surg* 2010;**251**:323–9.
30. Chann YC. Improving hospital cost accounting with activity-based costing. *Health Care Manage Rev* 1993;**18**:71–7.